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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE MAR - 1 2002

TECH CENTER 1600/2900

Applicant: H. Robert Horvitz et al.

Art Unit: 1654

Serial No.: 09/888,243

Examiner:

Filed: June 22, 2001

Customer No.: 21559

Title: Relatedness of Human Interleukin-1beta Convertase Gene to a C.  
Elegans Cell Death Gene, Inhibitory Portions of these Genes and Uses  
Therefor

Assistant Commissioner For Patents  
Washington, DC 20231

### INFORMATION DISCLOSURE STATEMENT

Applicant submits the references listed on the attached form PTO-1449.

Submission of this statement is not a representation that a search has been made,  
nor is information included in this statement an admission that the information is material  
to patentability.

Under 35 U.S.C. § 120, this application relies on the earlier filing date of  
application serial number 08/394,189, filed on February 24, 1995. The present  
references were submitted to and/or cited by the Office in the prior application and,  
therefore, are not provided in this application.

This statement is being filed before the receipt of a first Office Action on the merits.

If there are any other charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: February 7, 2002

Kristina Becker-Brady  
Kristina Becker-Brady, Ph. D.  
Reg. No. 39,109

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Clark & Elbing LLP  
176 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



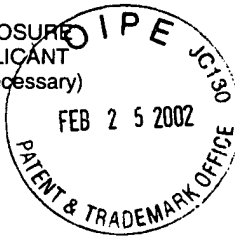
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| SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE<br>(MODIFIED)<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br>(Use several sheets if necessary)<br><br>(37 CFR §1.98(b)) | Attorney Docket No. | 01997/211003            |
|  | Serial No.          | US 09/888,243           |
|  | Applicant           | H. Robert Horvitz et al |
|  | Filing Date         | June 22, 2001           |
|  | Group               | 1654                    |
|  | IDS Filed           | February 7, 2002        |
|  | Customer Number     | 21559                   |



**U.S. PATENTS**

| Examiner's Initials | Patent Number | Issue Date | Patentee        | Class | Subclass | Filing Date (If Appropriate) |
|---------------------|---------------|------------|-----------------|-------|----------|------------------------------|
|                     | 5,416,013     | 5/15/95    | Black et al.    | 435   | 226      |                              |
|                     | 5,278,061     | 1/11/94    | Bull et al.     | 435   | 212      |                              |
|                     | 5,492,824     | 2/20/96    | Talanian et al. | 435   | 226      |                              |

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**FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION**

| Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation (Yes/No) |
|-----------------|------------------|--------------------------|-------|----------|----------------------|
| WO 91/19007     | 12.12.91         | PCT                      |       |          |                      |
| WOA 920 7071    | 30.04.92         | PCT                      |       |          |                      |
| WOA 911 5577    | 17.10.91         | PCT                      |       |          |                      |
| EPA 053 3350    | 24.03.93         | Europe                   |       |          |                      |

**OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)**

|   |
|---|
| Black et al., "Activation of interleukin-1 $\beta$ by a co-induced protease", FEBS LETTERS 247(2):386-390 (1989).   |
| Black et al., "A Pre-aspartate-specific Protease from Human Leukocytes that Cleaves Pro-interleukin-1 $\beta$ ", J. Biol. Chem. 264(10):5323-5326 (1989).   |
| Brenneman et al., "Cytokine Regulation of Neuronal Survival", J. Neurochem. 58(2):454-460 (1992).   |
| Cerretti et al., "Molecular Cloning of the Interleukin-1 $\beta$ Converting Enzyme", Science 256:97-100 (1992).   |
| Colotta et al., "Modulation of Granulocyte Survival and Programmed Cell Death by Cytokines and Bacterial Products", Blood 80(8):2012-2020 (1992).   |
| Estrov et al., "Suppression of Chronic Myelogenous Leukemia Colony Growth by Interleukin-1 (IL-1) Receptor Antagonist and Soluble IL-1 Recept.: A Novel Application for Inhibitors of IL-1 Activity", Blood 78(6):1476-1484 (1991). |
| Fuhlbrigge et al., "Molecular Biology and Genetics of Interleukin-1", Year Immunol. 5:21-37 (1989).   |
| Hogquist et al., "Interleukin 1 is Processed and Released During Apoptosis", Proc. Natl. Acad. Sci. USA 88:8485-8489 (1991).  |
| Horvitz and Chalfie, "Implications of Nematode Neuronal Cell Death for Human Neurological Disorders" in Neurodegenerative Disorders: Mechanisms and Prospects for Therapy, Price et al., (eds.) John Wiley & Sons, (1991) pp. 5-19. |
| Jacobson et al., "Breaking the ICE" Current Biology 4(4):337, 1994.   |
| Kostura et al., "Identification of a monocyte specific pre-interleukin 1 $\beta$ convertase activity", Proc. Natl. Acad. Sci. USA 86:5227-5231 (1989).  |

|   |                 |
|---|-----------------|
| EXAMINER  | DATE CONSIDERED |
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**OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)**

|  |  |
|--|--|
|  | Kronheim et al., "Purification of Interleukin-1 $\beta$ Converting Enzyme, the Protease that Cleaves the Interleukin-1 $\beta$ Precursor", Archives of Biochemistry and Biophysics 296:698-703 (1992).                       |
|  | Kumar et al., "Identification of a Set of Genes with Developmentally Down-Regulated Expression in the Mouse Brain", Biochem. Biophys. Res. Comm. 185(3):1155-1161 (1992).  |
|  | Ledoux et al., "Isolation of nematode homologs of the C. elegans cell death gene ced-3" Neurobiology of Aging 13:S47 (1992).   |
|  | Lotem and Sachs, "Hematopoietic Cytokines Inhibit Apoptosis Induced by Transforming Growth Factor $\beta$ 1 and Cancer Chemotherapy Compounds in Myeloid Leukemic Cells", Blood 80(7):1750-1757 (1992).                      |
|  | Mangan and Wahl, "Differential Regulation of Human Monocyte Programmed Cell Death (Apoptosis) by Chemotactic Factors and Pro-Inflammatory Cytokines", J. Immun. 147(10):3408-3412 (1991).                                    |
|  | Mangan et al., "IL-4 Enhances Programmed Cell Death (Apoptosis) in Stimulated Human Monocytes", J. Immun. 148(6):1812-1816 (1992).   |
|  | Mangan et al., "Lipopolysaccharide, Tumor Necrosis Factor- $\alpha$ and IL-1 $\beta$ Prevent Programmed Cell Death (Apoptosis) in Human Peripheral Blood Monocytes", J. Immun. 146:1541-1546 (1991).                         |
|  | McConkey et al., "Agents that Elevate cAMP Stimulate DNA Fragmentation in Thymocytes", J. Immun. 145(4):1227-1230 (1990).  |
|  | McConkey et al., "Interleukin 1 Inhibits T Cell Receptor-Mediated Apoptosis in Immature Thymocytes", J. Biol. Chem. 265(6):3009-3011 (1990).   |
|  | (Merck & Co. Inc.) Database WPI Week 9318 AN 93-144400 February 1993 Abstract, Derwent Publications Ltd. London, GB  |
|  | Miller et al., "The IL-1 $\beta$ Converting Enzyme as a Therapeutic Target" Ann. NY Acad. Sci. 696:133, 1993.  |
|  | Miura et al., "Induction of Apoptosis in Fibroblasts by IL-1 $\beta$ -Converting Enzyme, a Mammalian Homolog of the C. elegans Cell Death Gene ced-3" Cell 75:653, 1993.   |
|  | Molineaux et al., "Interleukin 1 $\beta$ (IL-1 $\beta$ ) processing in murine macrophages requires a structurally conserved homologue of human IL-1 $\beta$ ", Proc. Natl. Acad. Sci. USA 90:1809-1813 (1993).               |
|  | Nett et al., "Molecular Cloning of the Murine IL-1 $\beta$ Converting Enzyme cDNA", J. Immun. 149:3254-3259 (1992).  |
|  | Pickup et al., "Hemorrhage in Lesions Caused by Cowpox Virus is Induced by a Viral Protein that is Related to Plasma Protein Inhibitors of Serine Proteases", Proc. Natl. Acad. Sci. USA 83:7698-7702 (1986).                |
|  | Rambaldi et al., "Modulation of Cell Proliferation and Cytokine Production in Acute Myeloblastic Leukemia by Interleukin-1 Receptor Antagonist and Lack of its Expression by Leukemic Cells", Blood 78(12):3248-3253 (1991). |

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U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

Attorney Docket No.

01997/211003

Serial No.

US 09/888,243

Applicant

H. Robert Horvitz et al

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(37 C.F.R. §1.98(b))

## OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)

Ray et al., "Viral Inhibition of Inflammation: Cowpox Virus Encodes an Inhibitor of the Interleukin-1 $\beta$  Converting Enzyme", Cell 69:597-604 (1992).Sleath et al., "Substrate Specificity of the Protease that Processes Human Interleukin-1 $\beta$ ", J. Biol. Chem. 265(24):14526-14528 (1990).Thornberry et al., "A Novel Heterodimeric Cysteine Protease is required for Interleukin-1 $\beta$  Processing in Monocytes", Nature 356:768-774 (1992).

Wang et al., "Ich-d1, and ice/ced-3-Related Gene, Encodes Both Positive and Negative Regulators of Programmed Cell Death" Cell 78:739, 1994.

Yuan, J., Dissertation Abstracts International, Vol. 50/10-B, (1989).

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